124. (New) A method for grouping measured response profiles in sets which are associated with similar biological effects comprising grouping response profiles among a plurality of response profiles into sets, each of said sets of response profiles consisting of response profiles in which the responses of one or more sets of cellular constituents in each response profile are similar among response profiles in the set, each response profile in said plurality of response profiles (i) comprising measurements of a plurality of cellular constituents, and (ii) resulting from a different drug perturbation, wherein each of said sets of cellular constituents consists of cellular constituents that co-vary under a plurality of perturbations or that are co-regulated.

REMARKS

Claims 1, 3-50, 58-64, 72-78, and 89-106 were pending in the application after the filing of the May 22, 2001 Amendment. In the instant Supplemental Amendment claims 101-104 have been canceled, claims 1, 6, 30, 44, 50, 72-74, 76, 100 and 105 have been amended, and new claims 107-124 have been added, to more particularly point out and distinctly claim the invention. Upon entry of the above-made amendments, claims 1, 3-50, 58-64, 72-78, 89-100, and 105-124 will be pending. A marked version of the claims indicating the changes to the claims is attached hereto as Exhibit A. A clean version of the pending claims, as amended, is attached hereto as Exhibit B.

Claims 1, 6, and 30 have been amended to recite that the first plurality of perturbations are *drug* perturbations, whereas claim 100 has been amended to recite that the claimed method is for grouping sets of *drug* perturbations that similarly affect cellular constituents (emphasis added). Support for the amendments is found in the specification at page 5, lines 9-15; page 14, line 22 through page 15, line 4; page 15, lines 9-16; page 16, lines 7-21; page 41, line 25 through page 43, line 22; and FIG. 1. Claim 6 has also been amended to correct a grammatical error.

Claims 44, 50, and 72-74 have been amended to recite that the cellular constituents are *genes* and the response profiles comprise measurements of *transcript levels of a plurality of genes* (emphasis added). Support for the amendments is found in the specification at page 4, lines 28-30; page 6, lines 6-17; page 16, line 28 through page 17, line 17; and FIGS. 2 and 3.

Claim 105 has been amended to be in independent form including all of the limitations of the base claim.

New claims 107-124 have been added to more particularly point out the present invention. Support for new claims 107-110 is found in the specification at page 15, lines 6-8. Support for new claims 111-114 is found in the specification at page 14, lines 14-21. Support for claims 115-123 is found in the specification at page 23, line 15 through page 34, line 20. Support for claim 124 is found in the specification at page 16, lines 7-21.

No new matter has been added by the amendments and the new claims. Entry of the foregoing amendments and remarks is respectfully requested.

CONCLUSION

Applicants respectfully request entry of the foregoing amendments and remarks into the file of the above-identified application. Applicants believe that the claims as amended more particularly point out and distinctly claim the present invention, and that all the pending claims are in condition for allowance. Allowance of the application is respectfully requested.

Respectfully submitted,

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EXHIBIT A: MARKED VERSION OF THE AMENDED CLAIMS
U.S. APPLICATION SERIAL NO. 09/220,142
(ATTORNEY DOCKET NO. 9301-035-999)

(as amended July 30, 2001)

1. (Four Times Amended) A method of determining a consensus profile for a first plurality of drug perturbations to a cell type or organism, said method comprising identifying among a plurality of sets of cellular constituents in a plurality of response profiles one or more sets of cellular constituents, each of said one or more sets of cellular constituents being upregulated or downregulated by said first plurality of drug perturbations, each response profile in said plurality of response profiles (i) comprising measurements of a plurality of cellular constituents, and (ii) resulting from a different drug perturbation to said type of cell or organism, wherein each set of cellular constituents in said plurality of sets of cellular constituents consists of cellular constituents that co-vary under a second plurality of perturbations or that are co-regulated, wherein said plurality of response profiles comprises at least five response profiles, and wherein said consensus profile for said first plurality of drug perturbations comprises measurements of said one or more sets of cellular constituents.

6. (Three Times Amended) The method of claim 1, wherein said first plurality of drug perturbations [are] is associated with a particular biological effect.

30. (Three Times Amended) The method of claim 1 wherein the consensus profile is the intersection of the sets of cellular constituents activated or de-activated by said first plurality of drug perturbations.

44. (Four Times Amended) A method for grouping measured response profiles in sets which are associated with similar biological effects comprising grouping response profiles among a plurality of response profiles into sets, each of said sets of response profiles consisting of response profiles in which the responses of one or more sets of [cellular constituents] genes in each response profile are similar among response profiles in the set, each response profile in said plurality of response profiles (i) comprising measurements of transcript levels of a plurality of [cellular constituents] genes, and (ii) resulting from a

different perturbation, wherein each of said sets of [cellular constituents] genes consists of [cellular constituents] genes that co-vary under a plurality of perturbations or that are co-regulated, wherein said plurality of response profiles comprises at least five response profiles.

50. (Amended) The method of claim 49, wherein the objective statistical test comprises:

(a) determining an actual fractional improvement in the cluster analysis of the response profiles;

(b) generating permuted response profiles by means of Monte Carlo randomization of [cellular constituent] gene index for each response profile across the measured [cellular constituents] genes;

(c) performing cluster analysis on the permuted response profiles;

(d) determining the fractional improvement in the cluster analysis of the permuted response profiles; and

(e) repeating said steps of generating permuted response profiles and performing cluster analysis on the permuted response profiles so that a distribution of fractional improvements is obtained;

wherein the statistical significance is determined by comparing the actual fractional improvement to the distribution of fractional improvements.

72. (Three Times Amended) A method for analyzing response data from a biological sample comprising

(a) grouping cellular constituents from the biological sample into sets of [cellular constituents] genes that co-vary in a plurality of response profiles, each response profile in said plurality of response profiles (i) comprising measurements of transcript levels of a plurality of [cellular constituents] genes, and (ii) resulting from a different perturbation to said biological sample; and

(b) grouping the plurality of response profiles into sets of response profiles that similarly affect [cellular constituents] genes,

wherein said plurality of response profiles comprises at least five response profiles.

73. (Amended) The method of claim 72, wherein one or more [cellular constituents] genes which co-vary in association with a particular biological effect are identified from the sets of [cellular constituents] genes that co-vary in said plurality of response profiles.

74. (Amended) The method of claim 72, wherein one or more response profiles that are associated with a particular biological effect are identified from the sets of response profiles that similarly affect [cellular constituents] genes.

76. (Amended) The method of claim 73, wherein [the cellular constituents from the biological sample comprise a plurality of genes or gene transcripts, and] one or more genes associated with said biological effect are identified.

100. (Three Times Amended) A method of grouping sets of drug perturbations that similarly affect cellular constituents in a cell type or organism among a plurality of drug perturbations comprising grouping response profiles among a plurality of response profiles in sets, each of said sets of response profiles consisting of response profiles in which the responses of one or more sets of cellular constituents are similar among the response profiles in the set, each response profile in said plurality of response profiles (i) comprising measurements of a plurality of cellular constituents, and (ii) resulting from a different drug perturbation, wherein each of said sets of cellular constituents consists of cellular constituents that co-vary under a plurality of perturbations or that are co-regulated, thereby grouping said sets of drug perturbations, wherein said plurality of response profiles comprises at least five response profiles.

Claims 101-104 are canceled.

105. (Amended) [The method of claim 101] A method for grouping measured response profiles in sets which are associated with similar biological effects comprising grouping response profiles in sets among a plurality of response profiles by cluster analysis of said plurality of response profiles, said sets of response profiles consisting of response profiles having similar responses of a group of cellular constituents, each response profile in said plurality of response profiles (i) comprising measurements of a plurality of cellular

constituents, and (ii) resulting from a different perturbation, wherein a statistical significance for the sets of response profiles is determined by means of an objective statistical test.

New claims 107-124 are added.